reversed with treatment. As long as irreversible end-organ damage has not occurred (choroidal ischaemia *vs* choroidal infarction, or more commonly AION), treatment can restore perfusion and end-organ function.

References

1 Mack HG, O'Day J, Currie J. Delayed choroidal perfusion in giant cell arteritis. *J Clin Neuro-Ophthalmol* 1991; **11**: 221–227.
2 Hayreh SS, Podhajsky PA, Zimmerman B. Ocular manifestations of giant cell arteritis. *Am J Ophthalmol* 1998; **125**(4): 509–520.
3 Sivalingam A, Brown GC, Magargal LE. The ocular ischaemic syndrome. III. Visual prognosis and the effect of treatment. *Int Ophthalmol* 1991; **15**(1): 15–20.

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Sir,

Novel mutation in exon 2 of *COL2A1* gene in Japanese family with Stickler Syndrome type I

Stickler Syndrome (STL) is an autosomal dominant disorder characterized by degeneration of the vitreous and retina, and is frequently associated with myopia.[1] It is also accompanied by nonocular signs, such as orofacial anomalies, deafness, and arthritis. There are no widely accepted clinical diagnostic criteria for STL in ophthalmology.[2] Based on locus heterogeneity, a subclassification of STL has been proposed; *COL2A1* mutation associated STL type I with a congenital 'membranous' vitreous anomaly; *COL11A1* mutations associated with STL type II showing a 'beaded' phenotype; and *COL11A2* mutations associated with non-ocular STL type III (OMIM 120140, 120280, and 120290).[3] A subgroup of STL type I patients has been identified who are characterized by predominantly ocular disorders without systemic involvement.[4,5] It has been suggested that molecular genetics and scrutiny of the phenotype will provide evidence that clinicians require for accurate diagnosis.[2] However, several cases of STL with different degrees of severity and manifestations, and genetic background, have been reported mainly in the Western world.

Case report

We report on a 25-year-old Japanese woman who was referred to our clinic with a diagnosis of rhegmatogenous retinal detachment of the right eye. Family history revealed that her mother had undergone retinal detachment surgery in her forties. On the initial examination, her best-corrected visual acuity was 20/20 OU, and her refraction was −9.0 diopter sphere (DS) OD eye and −7.5 DS OS. Anterior-segment examination was unremarkable with clear lenses. Vitreous examination confirmed the presence of a type I membranous vitreous anomaly (Figure 1a and b). Ophthalmoscopy showed a horseshoe tear surrounded by a retinal detachment in the right peripheral retina, and circumferentially oriented lattice degenerations in both eyes. Atrophy of the retinal pigment epithelium, choriocapillaris and radial perivascular degeneration were not seen. No systemic abnormalities were found. We performed scleral buckling on the right eye and the detached retina was reattached.

Although we had tentatively diagnosed the proband with predominantly ocular STL type I based on her ocular features, we could not completely exclude other possibilities because of the unknown genetic a etiology of STL in the Eastern world. In addition, the absence of systemic involvement indicated that the patient had not met the criteria for the diagnosis of STL proposed by Snead.[1]

After obtaining informed consent, we performed direct sequencing of all coding regions of the *COL2A1* gene and found a heterozygous deletion of a G at position 237, which predicts a downstream premature stop codon in exon 5 of the *COL2A1* gene (accession number: NM001844) (Figure 2). Her mother, who declined ophthalmic examination, carried the same mutation in the *COL2A1* gene in the heterozygous state. This deletion was not detected in her father and 45 healthy controls.

Comments

Our study adds a novel mutation of the *COL2A1* gene to the existing mutations that causes STL type I. Based on the mutational analyses, we counseled our patient that her future children should undergo ophthalmic examinations and molecular analysis for earlier diagnosis or exclusion of STL. Our observations further supported the idea that, irrespective of race, mutations involving exon 2 of the *COL2A1* gene are characterized by a predominantly ocular STL phenotype.[4,5]

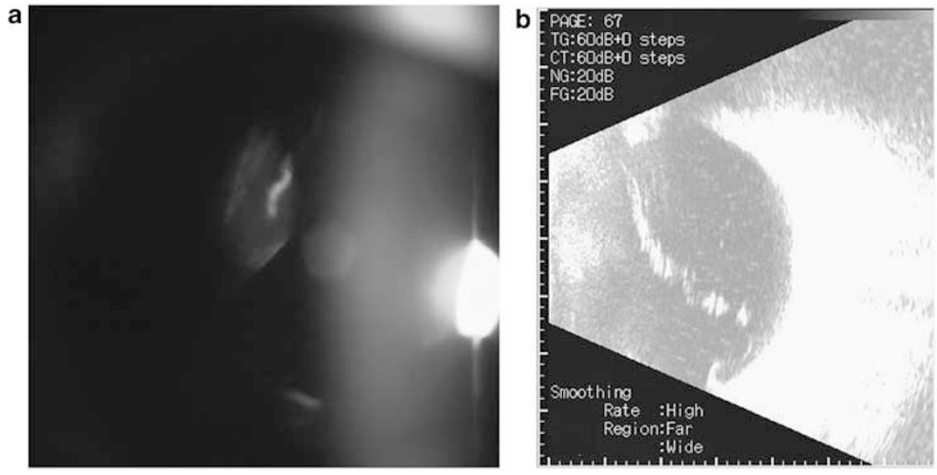

Figure 1 Slit-lamp photograph, ultrasonogram, and fundus photograph of the right eye. (a) Slit-lamp photograph (right eye) of the 25-year-old proband showing type I membranous vitreous anomaly. (b) B-mode ultrasonogram showing membranous vitreous that is set well back in the posterior segment of the right eye.

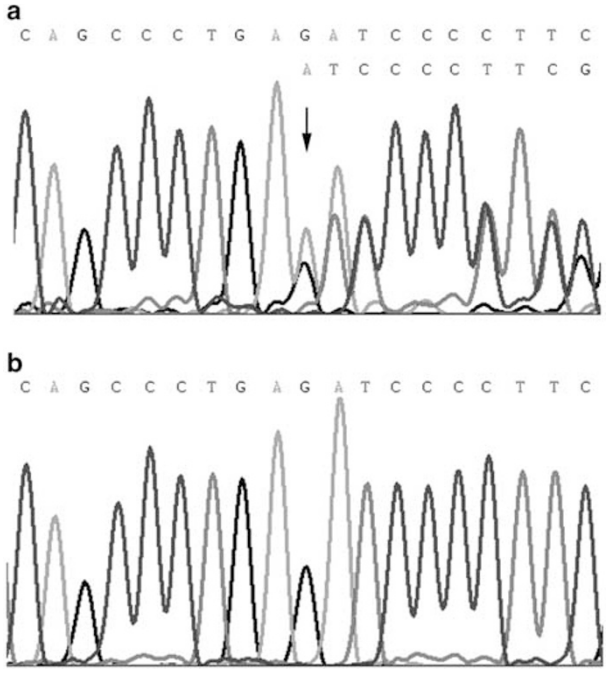

Figure 2 Direct sequence analysis of exon 2 of the *COL2A1* gene. (a) Arrow points to the heterozygous 1 bp deletion in exon 2 of the *COL2A1* gene identified in the proband and her mother which predicts a downstream premature stop codon in exon 5. This may lead to nonsense-mediated decay and haploinsufficiency. (b) No equivalent mutation was detected in her father or control subjects.

The existence of a predominantly ocular type of STL disorder may make an accurate diagnosis of the disease difficult, and the diagnosis of STL may be significantly overlooked in Japan. Although it has been proposed that radial perivascular retinal degeneration is a prominent feature of this predominantly ocular Stickler subset,[6] we did not observe this feature in our patient. Therefore, molecular genetic analysis of the *COL2A1* gene should be considered in routine clinical examination not only for accurate diagnosis of patients with predominantly ocular STL type I, but also for establishing reliable clinical diagnostic criteria.

Acknowledgements

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References

1 Snead MP, Yates JR. Clinical and molecular genetics of Stickler syndrome. *J Med Genet* 1999; **36**: 353–359.
2 Parke DW. Stickler syndrome: clinical care and molecular genetics. *Am J Ophthalmol* 2002; **134**: 746–748.
3 Richards AJ, Baguley DM, Yates JR, Lane C, Nicol M, Harper PS *et al*. Variation in the vitreous phenotype of Stickler syndrome can be caused by different amino acid substitutions in the X position of the type II collagen Gly-X-Y triple helix. *Am J Hum Genet* 2000; **67**: 1083–1094.
4 Richards AJ, Martin S, Yates JR, Scott JD, Baguley DM, Pope FM *et al*. COL2A1 exon 2 mutations: relevance to the Stickler and Wagner syndromes. *Br J Ophthalmol* 2000; **84**: 364–371.
5 Donoso LA, Edwards AO, Frost AT, Ritter R, Ahmad NN, Vrabec T *et al*. Identification of a stop codon mutation in exon 2 of the collagen 2A1 gene in a large stickler syndrome family. *Am J Ophthalmol* 2002; **134**: 720–727.
6 Parma ES, Korkko J, Hagler WS, Ala-Kokko L. Radial perivascular retinal degeneration: a key to the clinical

diagnosis of an ocular variant of Stickler syndrome with minimal or no systemic manifestations. *Am J Ophthalmol* 2002; **134**: 728–734.

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Sir,

Gyrate atrophy with bilateral full thickness macular hole

Gyrate atrophy of the choroid and retina, a rare autosomal recessive inborn error of amino-acid metabolism, is caused by mutation in the gene encoding the ornithine amino transferase with its onset in early childhood.[1] Ocular findings include axial myopia, posterior subcapsular cataract, and typical well-demarcated circumferential patches of chorioretinal atrophy with scalloped margins.[1] Choroidal neovascularization,[2] keratoconus,[3] cystoid macular edema, and epiretinal membrane formation[4] have also been reported. We report bilateral macular holes in a patient with gyrate atrophy, which to the best of our knowledge has been not described in the literature (MEDLINE Search).

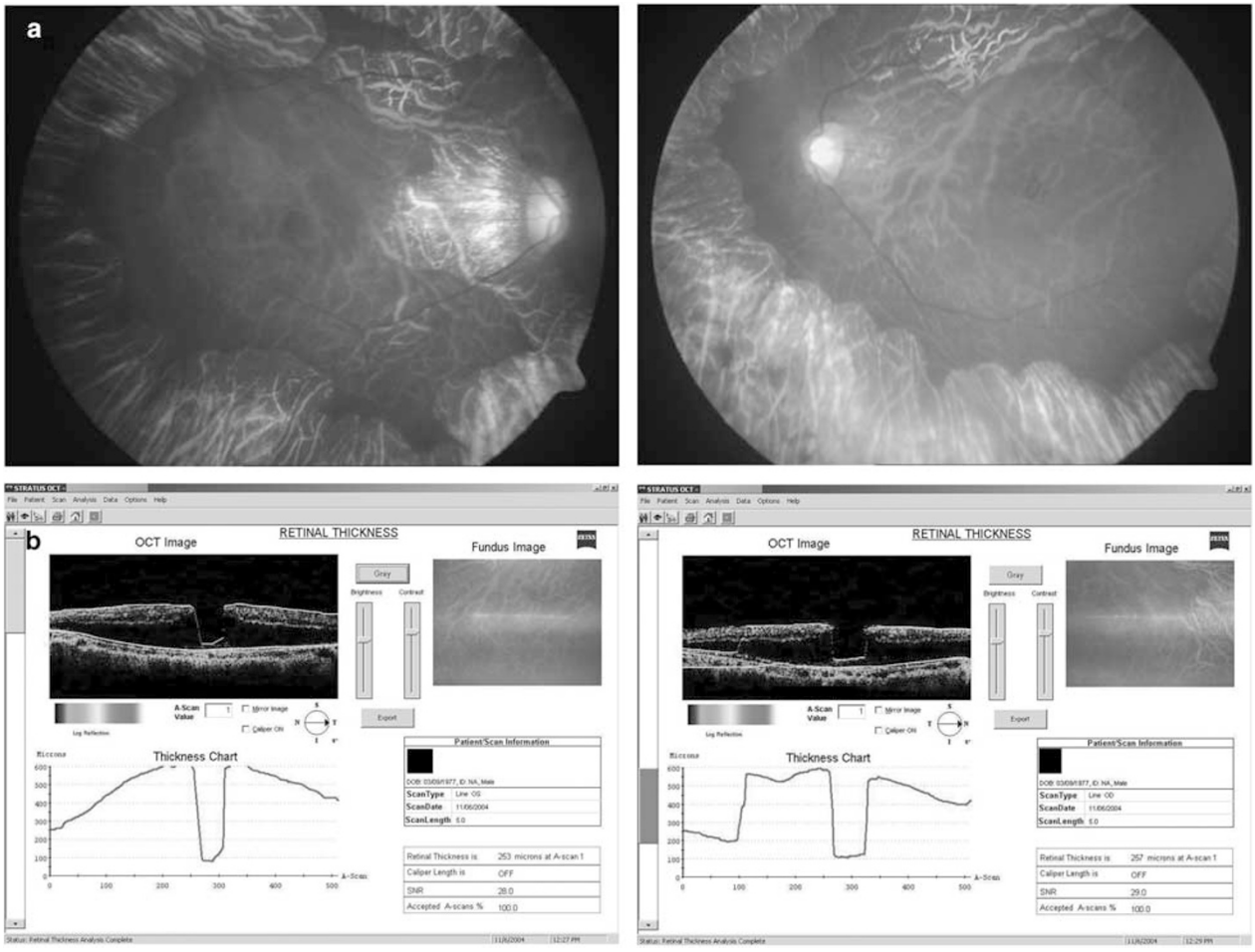

Figure 1 (a) Fundus photographs (top). Concentric chorioretinal atrophy with scalloped margins along with full thickness macular hole (FTMH) is seen in OD (top left) and OS (top right). (b) OCT Images (bottom). FTMH with surrounding neurosensory detachment can be seen in OD (bottom left) and OS (bottom right).